

### **Remarks**

The above Amendments and these Remarks are in reply to the Office Action mailed 18 October 2006. No fee is due for the addition of any new claims. An appropriate Petition for Extension of Time to Respond is submitted herewith, together with the appropriate fee.

Claims 1-51 were pending in the Application prior to the outstanding Office Action. In the Office Action, the Examiner rejected all claims. The present Response amends claims 1, 3-8, 10, 12, 16, 19-21, 23-26, 30-34, 36-44 and 48-51, leaving for the Examiner's present consideration claims 1-51. Reconsideration of the rejections is requested.

#### **I. REJECTION UNDER 35 USC 112**

The Examiner rejected claims 39-41 under 35 U.S.C. §112 because these dependent claims call for a medium whereas their parent claim 34 calls for a method.

This typographical error has been corrected.

#### **II. ART REJECTIONS**

The Examiner rejected claims 34, 36-46 and 48-51 as being anticipated by Brown. She also rejected claims 1-9, 35 and 47 as being obvious over a combination of Brown and Friedman, and rejected claims 10-33 as being obvious over a combination of Brown and Cunningham.

The Examiner and her supervisor are thanked for the courtesy of their interview with the undersigned on March 2, 2006. Most of the claim amendments above and comments below are made as a result of that interview.

As discussed generally during the interview, and as pointed out in Applicants' specification for example at paragraph [0036], an important aspect of the present patent application is directed to Applicants' concept that by forcing a protocol specification into a properly designed formal model of a protocol, operational uncertainties inherent in the protocol specification can be more easily uncovered before execution begins.

The concept is much like the concept of trying to fit square pegs into round holes. If one were to design the formal model as having numerous slot designs, each having its own shape, and then one were to consider a protocol specification as specifying numerous aspects, each with its own shape, and then one were to consider the encoding effort as the process of inserting all

the protocol specification pegs into their corresponding slots in the protocol model, then it can be seen that a specification aspect (peg) will not fit into the protocol database (slots) unless it has the proper shape. It can be seen that with proper design of the formal model (i.e. by providing the model with the right kinds of slots to be filled), the process of uncovering operational uncertainties in a protocol specification can be simplified to the process of inserting protocol specification pegs into the slots. If any protocol specification peg won't fit into its corresponding slot instantiated according to the model, then it is likely that an operational uncertainty has been discovered in the protocol specification.

It can be seen further that it is the act of placing all the pegs into slots, *i.e. the step of encoding*, which facilitates the identification of operational uncertainties. It is much harder to identify operational uncertainties by studying the pegs alone. For this reason, many of Applicants' claims call for the step of identifying an operational uncertainty to occur *during the step of encoding* a clinical trial protocol. If a prior art reference (such as Brown) teaches a step of identifying operational uncertainties, but does not teach that the step occurs *during a step of encoding* the protocol specification in accordance with a formal model, then it is unlikely that the prior art reference has any understanding of Applicants' concept above.

It can be seen further that the structure of the formal model (i.e. the kinds of slots that the formal model pre-specifies) in large part determines the kinds of operational uncertainties that Applicants' methodology will uncover. As mentioned in Applicants' specification for example at paragraph [0039], Applicants have determined that the temporal relationships among events that the protocol specifies to occur, are a particularly fertile area for operational uncertainties to arise. Some of Applicants' claims therefore are directed to particular features of the formal model (i.e. the use of certain kinds of slots), that are specifically designed to uncover operational uncertainties in temporal relationships that should be specified, and specified clearly and consistently, in the protocol specification. If a prior art reference (such as Brown) does not evidence a formal model that offers slots to be filled in specifically on the basis of information in the protocol specification about times specified to elapse between events also specified in the protocol specification, then it is unlikely that the prior art reference has any appreciation of the frequency with which temporal relationships that the protocol should specify between protocol events, give rise to operational uncertainties in clinical trial protocol specifications.

Finally, while Applicants' methodology can be performed during protocol execution, as pointed out in Applicants' specification for example at paragraphs [0026] and [0027], it is far more valuable when performed before the protocol is ever executed. Many of Applicants' claims therefore are limited to circumstances in which an operational uncertainties in the protocol specification is identified before execution of the protocol. If a prior art reference teaches all the other limitations of Applicants' claim, but does not identify operational uncertainties in the protocol specification until after a trial according to the protocol is already in progress, then it is unlikely that the prior art reference appreciates the significance of finding such operational uncertainties before the trial begins.

The above is provided by way of background and context, and is not intended to describe any claim limitations specifically. Applicants of course expect the Examiner to compare the claim language itself with the prior art.

Applicants will now discuss the independent claims in claim number sequence, followed by the dependent claims.

#### **A. Independent Claim 1**

The Examiner rejected claim 1 over Brown in view of Friedman.

During the interview, it was explained that the Examiner considered Brown's mention of ambiguities in suggested answers, to constitute "operational uncertainties" in a protocol, and that she considered the ability of Brown to change the protocol in response to the trend of the data, to satisfy the step of "encoding" a clinical trial protocol.

Claim 1 has been amended in light of the Examiner interview, as well as for other reasons. Applicants' comments below relate to the amended claim.

##### **1. "Operational Uncertainty" Excludes Brown's Data Ambiguities**

Applicants have now amended claim 1 to clarify that the term "operational uncertainties" is intended to cover only uncertainties in the protocol specification, not uncertainties in the data taken during protocol execution and not Brown's ambiguities in answers suggested by the protocol. In particular, claim 1 has been amended to call for a step of:

....identifying an operational uncertainty in which said protocol specification contains at least one of the following deficiencies: said protocol specification fails to specify a particular parameter for use during protocol execution, or said protocol specification specifies such a parameter too vaguely to be encoded into said database, or said protocol specification specifies such a parameter inconsistently....

Support for this language can be found in Applicants' specification, for example in paragraph [0104].

Nothing in Brown teaches or suggests identifying an uncertainty of any of the three types mentioned in Applicants' claim. Certainly nothing in Brown teaches or suggests identifying such an uncertainty in the protocol *specification*.

## 2. Claimed Steps Performed Before Protocol Execution

Applicants have amended claim 1 also to clarify that all the steps called for in the claim are to be performed *before the protocol is executed*. In particular, claim 1 now calls for steps of:

encoding into a database, workflow tasks called for in a clinical trial protocol specification not yet in execution, ....;

during said step of encoding workflow tasks called for in a clinical trial protocol specification not yet in execution, identifying an operational uncertainty ....;

encoding into said database in association with at least a particular one of said protocol specification objects in said database, before execution of said clinical trial protocol, ....; and

in dependence upon protocol specification objects in said database, before execution of said clinical trial protocol, displaying a graphical visual representation of said protocol, ....

Brown, by contrast, is almost completely unconcerned with activities that take place before execution of the protocol. The only steps that take place before protocol execution are steps 201-205 in Fig. 2a. The Examiner has pointed to the description accompanying step 205 as potentially teaching pre-execution review of the protocol, but that description (Brown, col. 6,

lines 13-18) says only that "[i]n alternative embodiments, the server device 130 may send the research and protocol 131 information to other medical research experts 121 for review." It does not say that they identify "operational uncertainties" in such review, and certainly not the specific kinds of uncertainties now called for in Applicants' claim.

3. Operational Uncertainty To Be Identified During Encoding of Protocol Tasks

Claim 1 also calls for the step of identifying the operational uncertainty "during the step of encoding workflow tasks called for in a clinical trial protocol specification" not yet in execution. Brown clearly does not do this.

In particular, even if the medical research experts 121 do identify an operational uncertainty during the alternative embodiment of Brown's step 205, that identification would not have occurred *during the step of encoding* the clinical trial protocol, which the Examiner has identified as occurring in Brown's earlier step 202.

Moreover, as mentioned above, Brown's failure to identify issues *during the step of encoding*, demonstrates that Brown has *no understanding at all* of Applicants' concept that by forcing a protocol specification into a properly designed formal model of a protocol, operational uncertainties can be more easily uncovered before execution begins.

Claim 1 as amended therefore distinguishes over the combination of Brown and Friedman for at least three reasons: (1) Brown fails to teach or suggest Applicants' step of "identifying an operational uncertainty"; (2) Brown fails to teach or suggest Applicants' claim limitations that each step be performed before protocol execution; and (3) Brown fails to teach or suggest Applicants' claim limitation that the operational uncertainty be identified during the step of workflow tasks called for in a clinical trial protocol specification not yet in execution.

Accordingly, it is respectfully submitted that claim 1 should be patentable.

**B. Independent Claim 10**

The Examiner rejected claim 10 as being obvious over a combination of Brown and Cunningham.

Claim 1 has been amended to call for, among other things, a database that includes:

a disambiguation comment object which identifies an operational uncertainty in which said protocol specification contains at least one of the following deficiencies: said protocol specification fails to specify a parameter for use during protocol execution, or said protocol specification specifies such a parameter too vaguely to be encoded into said database, or said protocol specification specifies such a parameter inconsistently

As pointed out above with respect to claim 1, Brown neither teaches nor suggests that his database include an object which identifies an "operational uncertainty" in which the protocol specification contains any of the three specific types of deficiencies called for in the claim.

Accordingly, it is respectfully submitted that independent claim 10 should be patentable.

### **C. Independent Claim 23**

The Examiner rejected claim 23, too, as being obvious over a combination of Brown and Cunningham.

Claim 23 has been amended to call for a set of media carrying, among other things, "a plurality of machine readable objects instantiated according to a pre-specified class structure, the machine readable objects including protocol event specification objects describing protocol events that a protocol specification specifies to occur during execution of said protocol".

Neither Brown nor Cunningham mention the use of a pre-specified class structure, and for that reason the combination immediately fails to teach a limitation of Applicants' claim.

They certainly do not teach the use of such a pre-specified class structure to define "protocol event specification objects describing protocol events that a protocol specification specifies to occur during execution of said protocol".

Nor is the limitation suggested, because as explained above, it is the pre-specified class structure which provides the "round holes" that the "pegs" of the protocol specification must fit into. Without a pre-specified class structure, it is extremely unlikely that either Brown or Cunningham has any understanding of Applicants' concept that operational uncertainties in a protocol specification can be more easily discovered during the step of encoding the protocol specification into a properly designed formal protocol model (i.e. fitting the pegs into the slots).

Claim 23 also calls for the objects instantiated according to this class structure to include "temporal constraint specification objects describing temporal relationships that a protocol specification specifies to occur among protocol events described in said protocol event specification objects, at least a particular one of said temporal constraint specification objects identifying an amount of time that said protocol specifies is to elapse between two or more protocol events when the protocol is executed." But nothing in Brown teaches that his database includes such "temporal constraint specification objects".

The Examiner has argued, as Applicants understand it, that temporal constraints are inherent in Brown because a clinical trial is always concerned with the progression of an illness or other condition over time. As an example, the Examiner has suggested that a clinical trial might include a question, to be asked of a patient, such as "How did you feel 6 hours after you took the pill?"

But the Examiner's hypothetical question is not at all inherent in Brown, nor are questions like it. Many clinical trials do not include such questions. Inherency requires that the allegedly inherent teaching *necessarily* flows from the teachings of the applied prior art (MPEP 2112), which is clearly not the case as regards Brown.

It is certainly not inherent in Brown that such temporal relationships be encapsulated in objects "instantiated according to a pre-specified class structure," as called for in Applicants' claim. If the Examiner believes Brown does teach this limitation, it is respectfully requested that she point out the class structure in Brown based on which such objects are instantiated.

And even more importantly, the claim calls for the machine readable objects to include "temporal constraint specification objects describing temporal relationships that a protocol specification specifies to occur among protocol events described in protocol event specification objects", which according to the claim describe "protocol events that a protocol specification specifies to occur during execution of said protocol."

Thus in order for the 6 hour time period in the Examiner's example question to satisfy the limitations of Applicants' claim, the time period would have to occur between protocol events *that a protocol specification specifies to occur during execution of said protocol*, and it would have to be specified as a temporal relationship *that the protocol specification specifies to occur* between such protocol events. An example is a protocol specification that the patient is to be

called back for a next office visit 6 days after the previous office visit, where each of the visits are specified in "protocol event specification objects", and the 6-day time period is specified in a "temporal constraint specification object". The 6 hour time period in the Examiner's example question does *not* satisfy the limitations of Applicants' claim unless (1) both the taking of the pill and the patient's noting how he or she feels, are both specified by the protocol specification; (2) both events are described in "protocol event specification objects" as events that are to occur; (3) the protocol specification specifies that 6 hours are to elapse between the two events; (4) the 6-hour time period is described in a "temporal constraint specification object" relating the two events together; and (5) all the objects are "instantiated according to a pre-specified class structure."

While a protocol specification could conceivably be encoded in this manner, Applicants respectfully submit that nothing in Brown suggests or makes it inherent that Brown has done so. It is not at all clear from Brown that all of these conditions *necessarily* flow from the teachings of Brown.

Nor is the temporal constraint limitation of Applicants' claim in any way obvious from Brown. As mentioned above, this limitation is based on Applicants' appreciation that such temporal relationships represent a fertile ground for operational uncertainties in protocol specifications, and that by incorporating temporal constraint specification objects as called for in the claim, Applicants' methodology can be used effectively to uncover them.

Brown evidences no concept that protocol specifications can contain operational uncertainties in the temporal relationships that the protocol specifies among protocol events, much less teach their discovery by using "temporal constraint specification objects", "instantiated according to a pre-specified class structure", "identifying an amount of time that said protocol specifies is to elapse between two or more protocol events when the protocol is executed."

Accordingly, it is respectfully submitted that claim 23 should be patentable. It is further respectfully requested that if the Examiner wishes to make an inherency argument based on the teachings of Brown, that she do so with the full rigor required under MPEP 2112.

#### **D. Independent Claim 34**

The Examiner rejected claim 34 as being anticipated by Brown.



Claim 34 has been amended in light of the interview, as well as for other reasons. Claim 34 should now be patentable for many of the reasons set forth above with respect to independent claim 1.

In particular, Applicants have amended claim 34 to clarify that the "operational uncertainties" covered by the claim include only uncertainties in the protocol specification, and only uncertainties:

in which said protocol specification contains at least one of the following deficiencies: said protocol specification fails to specify a parameter for use during protocol execution, or said protocol specification specifies such a parameter too vaguely to be encoded into said database, or said protocol specification specifies such a parameter inconsistently.

Nothing in Brown teaches or suggests identifying an uncertainty of any of the three types mentioned. Certainly nothing in Brown teaches or suggests identifying such an uncertainty in the protocol *specification*.

Applicants also have amended claim 34 also to clarify that all the steps called for in the claim are to be performed *before the protocol is executed*. In particular, claim 1 now calls for steps of:

encoding into a database, workflow tasks called for in a clinical trial protocol specification not yet in execution, ...; and  
during said step of encoding, identifying an operational uncertainty ....

In Brown, by contrast, the only steps that take place before protocol execution are steps 201-205 in Fig. 2a. The description accompanying step 205 does *not* teach that Brown's medical research experts 121 identify "operational uncertainties" in their review of the protocol, and certainly not the specific kinds of uncertainties now called for in Applicants' claim.

Claim 34 also calls for the step of identifying the operational uncertainty "during the step of encoding workflow tasks called for in a clinical trial protocol specification" not yet in execution. As set forth with respect to claim 1, Brown clearly does not do this.

In particular, even if the medical research experts 121 do identify an operational uncertainty during the alternative embodiment of Brown's step 205, that identification would not have occurred *during the step of encoding* the clinical trial protocol, which the Examiner has identified as occurring in Brown's earlier step 202.

In addition to these reasons, claim 34 also calls for the database into which the workflow tasks called for in a clinical trial protocol to be encoded, be:

structured according to a predetermined model, said model including slots predefined for describing respective aspects of protocol events that a protocol can specify to occur during execution of the protocol, said model further including slots predefined for describing temporal relationships that a protocol can specify among such protocol events, said slots predefined for describing temporal relationships including slots predefined for describing amounts of time that a protocol specifies are to elapse between two or more protocol events;

As pointed out above with respect to claim 23, nothing in Brown teaches that his database is structured according to a predetermined model, nothing in Brown teaches that such a predetermined model include slots predefined for describing temporal relationships that a protocol can specify among such protocol events, and nothing in Brown teaches that any such slots are predefined for describing amounts of time that a protocol specifies are to elapse between two or more protocol events.

Nor are these limitations in any way obvious from Brown. As mentioned above, Brown evidences no concept that protocol specifications can contain operational uncertainties in the temporal relationships that the protocol specifies among protocol events, much less teach their discovery by encoding the protocol specification into a model offering slots predefined for discovering such uncertainties. Because Brown clearly does not have this concept, nothing in Brown can suggest that his teachings be modified to include all the above limitations.

Accordingly, since Brown fails to teach any of these limitations called for in Applicants' claim 34, it is respectfully submitted it cannot anticipate ant that the claim should be patentable.

**E. Independent Claim 42**

The Examiner rejected claim 42 as being anticipated by Brown.

Claim 42 has been amended in light of the interview, as well as for other reasons. Claim 42, too, should now be patentable for many of the reasons set forth above with respect to independent claim 1.

In particular, Applicants have amended claim 34 to clarify that the "operational uncertainties" covered by the claim include only uncertainties in the protocol specification, and only uncertainties:

in which said protocol specification contains at least one of the following deficiencies:  
said protocol specification fails to specify a parameter for use during protocol execution,  
or said protocol specification specifies such a parameter too vaguely to be encoded into  
said database, or said protocol specification specifies such a parameter inconsistently.

Nothing in Brown teaches or suggests identifying an uncertainty of any of the three types mentioned. Certainly nothing in Brown teaches or suggests identifying such an uncertainty in the protocol *specification*.

Applicants also have amended claim 42 also to clarify that all the steps called for in the claim are to be performed *before the protocol is executed*. In particular, claim 1 now calls for steps of:

encoding into a database, workflow tasks called for in a clinical trial protocol specification not yet in execution, ...;

during said step of encoding workflow tasks called for in a clinical trial protocol specification not yet in execution, identifying an operational uncertainty ...;

encoding into said database ..., before execution of said clinical trial protocol, an indication that said operational uncertainty exists....; and

in dependence upon objects in said database, before execution of said clinical trial protocol, outputting a report ....

In Brown, by contrast, the only steps that take place before protocol execution are steps 201-205 in Fig. 2a. The description accompanying step 205 is not to the contrary.

Claim 42 also calls for the step of identifying the operational uncertainty "during the step of encoding workflow tasks called for in a clinical trial protocol specification" not yet in execution. As set forth with respect to claim 1, Brown clearly does not do this.

Accordingly, since Brown fails to teach any of these limitations called for in Applicants' claim 42, it is respectfully submitted it cannot anticipate and that the claim should be patentable.

#### **F. Dependent Claims 2-9, 11-22, 24-33, 35-41 and 43-51**

These claims all depend ultimately from one of the independent claims 1, 10, 23, 34 or 42. Where necessary to ensure a proper antecedent basis, they have been amended to conform to the amendments made in their respective parent independent claim.

Applicants have reviewed the grounds for rejection of these claims as stated by the Examiner and respectfully do not agree with the positions taken. Nevertheless Applicants do not believe it necessary to discuss their views on these claims further, since these claims all depend ultimately from allowable independent claims. The dependent claims therefore are believed to be patentable for at least the same reasons as their respective ultimate parent claims.

In addition, these claims each add their own limitations which, it is submitted, render them patentable in their own right. For example, some of the dependent claims which depend from one independent claim, add limitations similar to those discussed above with respect to other independent claims, and these dependent claims should be patentable for similar reasons.

Accordingly, claims 43-51 are believed to be patentable.

### **III. CONCLUSION**

The references cited by the Examiner but not relied upon have been reviewed, but are not believed to render the claims unpatentable, either singly or in combination.

In light of the above, it is respectfully submitted that all of the claims now pending in the subject patent application should be allowable, and a Notice of Allowance is requested. The

Examiner is respectfully requested to telephone the undersigned if he can assist in any way in expediting issuance of a patent.

Enclosed is a PETITION FOR EXTENSION OF TIME UNDER 37 C.F.R. § 1.136 for extending the time to respond up to and including 18 April 2006.

The Commissioner is authorized to charge any underpayment or credit any overpayment to Deposit Account No. 50-0869 (FSTK 1004-1) for any matter in connection with this response, including any fee for extension of time, which may be required.

Respectfully submitted,

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